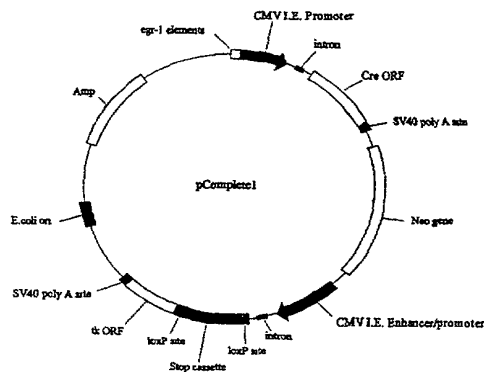




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/85, A61K 48/00, C12N 15/52, 15/53, 9/00, 9/02		A2	(11) International Publication Number: WO 99/60142
			(43) International Publication Date: 25 November 1999 (25.11.99)
(21) International Application Number: PCT/GB99/01362		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 17 May 1999 (17.05.99)		Published Without international search report and to be republished upon receipt of that report.	
(30) Priority Data: 9810423.5 15 May 1998 (15.05.98) GB			
(71) Applicant (for all designated States except US): CANCER RESEARCH CAMPAIGN TECHNOLOGY LIMITED [GB/GB]; Cambridge House, 6-10 Cambridge Terrace, Regent's Park, London NW1 4JL (GB).			
(72) Inventors; and (75) Inventors/Applicants (for US only): MARGISON, Geoffrey, Paul [GB/GB]; Hilltop Bungalow, Lyme Road, Poynton, Cheshire SK12 1TH (GB); MARPLES, Brian [GB/GB]; 19 Eskdale Avenue, Chesham, Bucks HP5 3AX (GB); SCOTT, Simon [GB/GB]; The Boston Cottage, Ballinger Common, Ballinger Road, Great Missenden, Bucks HP16 9LF (GB); HENDRY, Jolyon, Hindson [GB/GB]; Meadows, Brookledge Lane, Adlington, Macclesfield, Cheshire SK10 4JU (GB).			
(74) Agent: WILSON GUNN SKERRETT; Charles House, 148/9 Great Charles Street, Birmingham B3 3HT (GB).			

(54) Title: GENE THERAPY VECTORS AND THEIR USE IN ANTITUMOUR THERAPY



(57) Abstract

Vector material useful for antitumour therapy contains: (a) a tumour cell sensitizing gene or genes of which expression in a tumour cell yields a sensitizing gene expression product having a potential to cause tumour cells to be killed and destroyed, or to be eliminated, or otherwise to be inactivated, or to be rendered sensitive and/or vulnerable to destruction; (b) a sensitizing gene promoter; (c) at least one control gene; and (d) a control gene expression regulatory system responsive in use in a transfected cell to the effect of a predetermined exogenous or endogenous expression inducing influence, e.g. ionizing radiation, heat or a chemical inducing agent, so as to induce expression of the control gene to yield an expression product having a capacity to establish an operative linkage between the sensitizing gene promoter and the sensitizing gene or genes effective to trigger and switch on or permit continuous or permanent expression of the latter to bring about continuous production of the sensitizing gene expression product. This is preferably achieved by arranging for the control gene to encode a recombinase enzyme that acts on recombinase target sites in a Cre-loxP or Flp-frt site specific recombination system to remove an expression preventing stop cassette sequence between the sensitizing gene(s) and the promoter for the latter. In some embodiments the tumour sensitizing gene expression product will be an enzyme or other bioactive agent that can activate an inactive prodrug.